

Ill air slays sooner than the sword.

Ratis Raving, c. 1450

Forum

Breathing Easier

EPA scientists, with the support of the agency's Clean Air Scientific Advisory Committee (CASAC), have recommended limiting the amount of air particles that are 2.5 microns and smaller. Controlling these particles, known as PM_{2.5}, which come from burning coal and oil, should help millions of Americans breathe easier, says John Bachmann, the EPA's associate director for science policy and new program initiatives. Calling the recommendation to control PM_{2.5} "revolutionary," Bachmann says, "We'll be reducing risk to hundreds of millions of people. We hope to get a much greater and broader risk reduction than the strategies we used in the past that have tended to focus on the coarser particles," such as road dust and dirt particles.

Epidemiological studies have linked exposure to PM_{2.5} to a host of respiratory ailments and other health problems. Douglas Dockery, an epidemiologist at the Harvard School of Public Health, says, "Any place you look in the world, people have been able to see these associations between increased mortality, hospital admissions, increased emergency room visits, asthma attacks, increased reporting of respiratory symptoms, and decreased pulmonary function." The people most affected are those who already have respiratory health problems, Dockery added.

Echoing Dockery's concern is Ron White, the environmental health director of the American Lung Association. A number of epidemiological studies, he says, point to the danger posed by such minute particles. One such study is the Harvard Six Cities Study, headed by Dockery. Conducted over the last 20 years, the study found that a link exists between fine particulate air pollution and mortality.

Just how these fine particles cause adverse effects is uncertain, but the research of John Godleski of the Harvard School of Public Health points to a possible mechanism. Exposing laboratory rats to high concentrations of ambient air from around Boston, Godleski has found that healthy animals displayed no adverse effects. However, animals with experimentally induced bronchitis and lung inflammations died from exposure to the fine air particles. "That correlates well with the

epidemiological studies," Godleski says. But critics of the control recommendations are far from persuaded by such evidence.

Many epidemiological studies associating the PM_{2.5} with illness are based on faulty assumptions, says George Wolff, an atmospheric scientist with General Motors and chair of the CASAC. "Most of these studies use a central monitor in the cities and assume that the concentration measured [is] a measure of everybody's exposure," he said. Because pollution varies in cities, these results "may not accurately represent the actual exposure," he said.

Even if PM_{2.5} are found to be the culprit, Wolff challenges the effort to control them. "Do we have confidence that [this] will also reduce the specific component of the particle causing health problems," he questions. For instance, he says, it may be sulfuric acid on the particles that is causing negative health effects. "If you target a strategy to reduce primary emissions of particles, it wouldn't do any good," he says. "You have to target a strategy toward the precursor of sulfuric acid, sulfur dioxide, which is something the recommendation doesn't do."

University of Washington epidemiologist Suresh Moolgavkar argues that studies such as the Six Cities Study do not point in the direction that Dockery claims because they fail to control for factors like weather and other pollutants, and lead researchers to the conclusion that PM_{2.5} are responsible for respiratory illnesses and deaths. Furthermore, no biological mechanism has been described to account for the

symptoms associated with the particles, says lung specialist Mark Utell of the University of Rochester Medical Center, a CASAC member. The failure to pin down such a mechanism, he says, makes attempts to regulate the particles questionable. Utell is not satisfied that the fine particles alone can easily explain the increased deaths pointed to by epidemiological studies.

It will be up to EPA administrator Carol Browner to weigh such conflicting arguments and evidence and conclude whether to go ahead with the staff recommendation. Should she agree, the new standard will be proposed in the *Federal Register* and open for public comment by 29 November 1996. Unless Congress intervenes (it has 60 legislative days to "throw it back at us or let it go through," says Bachmann) the regulations would be promulgated by the end of June 1997. The EPA would then begin monitoring to see if the regulations are being met. Where they are not being met, steps to meet them would have to be taken. In those cases, it may be early in the next century before controls are implemented.

Preventing Lead Poisoning in China

The first childhood lead poisoning prevention center in China was dedicated with an International Symposium on Childhood Lead Poisoning Prevention held May 8–11 in Shanghai. The meeting was the first to bring clinicians and researchers from across China together to discuss childhood lead poisoning. China counts some 120 million children age six or younger (the age range at greatest risk for adverse effects of lead poisoning) in its population of 1.2 billion.

The symposium, sponsored by the Shanghai Second Medical University, the Shanghai Medical Association, and the Dr. Samuel Rosen Foundation, marked the official beginning of efforts to address the significant public health problem of lead exposure/lead poisoning for infants and other young children in China. A collaborative agreement signed in September 1995 helped



Getting underway. John F. Rosen and a translator present the history of the new Chinese center for prevention of childhood lead poisoning at its dedication.

lay the foundation for the new center, named the Montefiore Medical Center–Shanghai Institute for Pediatric Research Collaborating Center for Prevention of Childhood Lead Poisoning.

Xiaoming Shen, professor and director of the new center, led the symposium. Shen had helped to define the dimensions of the lead threat to Chinese children in a series of studies and surveys begun in the late 1980s by the Division of Lead Poisoning Prevention of the Shanghai Institute for Pediatric Research, under institute director Sheng-mei Wu, who coauthored some of the studies.

Shen had done postdoctoral training in pediatric lead research with John F. Rosen, director of the Division of Environmental Sciences at Montefiore Medical Center and Albert Einstein Medical College in New York City. Rosen is a long-time NIEHS grantee and a key figure in bringing childhood lead poisoning concerns to the attention of the Chinese medical and public health community.

Rosen, developmental psychologist David Bellinger of Harvard University and Children's Hospital in Boston, toxicologist Paul Mushak of PB Associates in Durham, North Carolina, and Kenneth Balbi, a visiting professor at Albert Einstein Medical College and director of training at PROTECT Franchising, Inc., and neurologist Yoram Finkelstein of Shaare Zedek Medical Center in Jerusalem were the official foreign delegation at the dedication and symposium. The group gave lectures covering low exposure health effects, exposure monitoring and modeling, environmental measurements, neurobehavioral effects, and toxic mechanisms.

Examination of 17 studies from different parts of China indicates that the prevalence of lead poisoning for children living in industrial and heavy traffic areas ranges from 64.9% to 99.5%, Shen said. As many as 50% of China's children living outside of such areas have lead poisoning (indicated by greater than 10 micrograms of lead per deciliter of blood).

Significant sources of lead for China's children include industrial emissions (often close to housing and schools), leaded gasoline, lead-contaminated toys and stationery, secondary occupational exposure that occurs when parents wear lead-contaminated clothing home from work, burning of coal for home heat and cooking, contaminated food, and some traditional medicines, according to Shen. China's rapid development and traffic growth have increased the potential for lead emissions, as has the growth of cottage industries that use lead.

EHPnet

The Inside Story

In July 1976, a faulty cooling tower allowed the pathogenic bacteria, *Legionella*, to be dispersed through the air conditioning system in a Philadelphia hotel, causing 182 of the guests there to become ill. Before the cause of the sickness had been discovered, 29 people had died. This is just one example of how the indoor human environment, which is designed to protect us from the hazards outside, can itself become deadly. In many parts of the world, office buildings house thousands of workers daily and an increasing number of people spend the majority of their time indoors. In addition to being potentially harmful to human health, the world's buildings can be extremely taxing on the earth's environment. Many heating, ventilation, and air conditioning systems are inefficient and, together with artificial lighting, constitute an enormous energy demand.

At Lawrence Berkeley National Laboratory's Center for Building Science (CBS), scientists face the challenge of

improving the ventilation and lighting systems of indoor environments while decreasing the amount of energy required to run them. The three separate research groups that comprise the center work in coordination with each other to develop energy-efficient technologies and analytical techniques for investigating indoor environments. The Building Technologies Program, the Energy Analysis Program, and the Indoor Environment Program each has its own home page on the World Wide Web, all of which can be accessed from the CBS home page located at <http://eande.lbl.gov/CBS/CBS.html>.

The Building Technologies Program conducts research involving indoor lighting systems and develops software for evaluating them. Links to the research groups located on this home page connect users to information on a number of public domain software packages for building designers, including SPARK, DOE-2, and Power DOE (programs that estimate the energy cost for a given building design) and WINDOW+5 and THERM (programs for evaluating the thermal and optical properties of windows).

The Energy Analysis Program examines worldwide energy use in a search for innovative and efficient end-use strategies. This research extends beyond building fixtures and appliances to the study of the urban environment. The Heat Island Project link, accessible through the Building Energy Analysis Group link on this home page, connects users to an informative reference on smog, evapotranspiration, and other environmental phenomena linked to urban heat islands. The results of important studies conducted by the Energy Analysis Program are also accessible from this home page, including a report that summarizes world commercial and industrial energy use, which can be downloaded by selecting the Industrial Energy Research link. Also included is a report on market characteristics for energy-efficient products found under the U.S. Energy End-Use Forecasting link. *Home Energy*, a journal of energy-efficient technology, is also located under the Building Energy Analysis link. The full text of articles from 1994 to the present can be accessed by a subject index or with a search engine linked to the magazine's home page.

The Indoor Environment Program studies indoor air pollutants including radon, volatile organic compounds, and combustion products, and analyzes their effects on human health. The site includes a list of recent publications that can be searched by following the Program Publications link. The results of the most recent research can also be accessed from the program's home page by following the Recent Research Highlights link. A complete index of current research taking place within the Indoor Environment Program is also available, including contacts' names.

The CBS home page also provides links to other sources of information on designing and living in healthy buildings. The Home Energy Saver link is the entrance to an expansive site that lets users analyze their homes for energy efficiency and provides information on how to save money on power bills. *The Center for Building Science News* is also linked to the CBS home page, with the full text of articles presented with graphics for issues from 1994 to present. The Energy Crossroads link connects users with an abundance of links to related sites.



**Lawrence Berkeley National Laboratory
Center for Building Science**



Allen Bale

Patches of pits. A recently identified gene called *patched* causes basal cell carcinomas, birth defects, and palmar pits.

Officials at the highest levels of China's government have recently recognized China's childhood lead poisoning problem. Shanghai Second Medical University was approved as the site for the poisoning prevention center early in 1996 by the Minister of Public Health, Min-zhang Chen. Preliminary work on raising awareness of the problem began in the late 1980s at the Shanghai Institute for Pediatric Research, following a series of professional interactions by Rosen and members of the Chinese medical community.

The Shanghai Institute for Pediatric Research sent a formal report on the lead problem to the Ministry of Health, said Di Guo, professor of pediatrics at Shanghai Second Medical University. "It is our hope that designation of the Montefiore Medical Center as a collaborating center and establishment of the [center] would prompt the prevention and research work on childhood lead poisoning in our country, thus promoting the health of our children," Guo said.

During their visit to China, Rosen, Mushak, and Bellinger met with Dakui Yin, the Chinese vice minister of health, and Ziren Xiao, secretary-general of the Chinese Medical Association, to discuss the dimensions and challenges of China's pediatric lead poisoning problem. The Chinese Medical Association served as the official host for the delegation visit in Beijing.

Members of the foreign delegation are expected to continue collaborations with Chinese colleagues in designing screening programs and lead-related pediatric health research.

Patched Gene Linked to Skin Cancer

Two recently published studies identify the gene that, when mutated, causes the most common form of cancer, basal cell carcinoma of the skin. The gene also causes a rare hereditary disease called Gorlin's disease, or basal cell nevus syndrome (BCNS). Basal cell carcinoma, which affects about 750,000 Americans each year, is curable by surgery if detected and treated early. BCNS, which affects about 1 in every 100,000 people, causes birth defects and the development of several types of cancers including basal cell carcinoma.

The gene, called *patched* or *ptc*, because of its patchy appearance of the mutant form of the gene, was first discovered in fruit flies, which are the best models for genetics, said Matthew Scott, a Howard Hughes investigator at Stanford University School of Medicine, who led one of the studies. The *patched* gene, or *PTCH*, is a human version of the fruit fly *patched* gene, one of a set of genes that determines how tissues are organized in the embryos of fruit flies. The human version of the gene is a tumor suppressor located on chromosome 9. Researchers believe that the gene mutation in humans is caused by exposure to ultraviolet light, which results in tumor growth. Cancer also results when the gene is defective or absent.

Scott and his colleagues, who were studying the *patched* gene and other fly developmental genes, found that a mutated version of the gene caused developmental problems in the fruit fly. They then located the gene in mice and humans and hypothesized that it could be the gene that, when mutated, causes BCNS. Scott con-

tacted a BCNS research team led by Ervin Epstein, Jr., at the University of California at San Francisco, and the two groups joined efforts. They confirmed that patients with BCNS did have the mutated gene. They also found the mutated gene in the tumors of patients with basal cell carcinoma, but they did not find it in the patients' nontumor cells. This finding supported the theory that the mutation was associated with basal cell carcinoma. Their work was published in the 14 June 1996 issue of *Science*.

Meanwhile, an international group of scientists led by Allen Bale, an associate professor of genetics at Yale University, also discovered the gene mutation in fruit flies and likewise linked it to BCNS and basal cell carcinoma. Bale said that the effort to isolate the BCNS gene has been ongoing since 1992 when the gene was mapped to human chromosome 9. Bale says he found it surprising that the fruit fly version of the gene is involved with the development of the embryo rather than with tumors. "Previous to this discovery, there was no evidence that a gene of this type could have anything to do with human cancer, and this finding helps tie together the birth defects and cancer predisposition seen in [BCNS]. Other human disorders characterized by both birth defects and cancer may be caused by similar genes," he said. The study led by Bale was published in the 14 June 1996 issue of *Cell*.

Scott said the discovery of the *patched* gene is significant because it contributes to the understanding of how genes work together. "Essentially, this gene ties us in to a whole set of genes which work to control growth and development," Scott said. He said that gaining knowledge about how the genes interact could lead to treatment methods. "There may be different points of the genetic pathway where we could intervene."

The researchers hope that the identification of the gene will lead to a better understanding of how cancer develops, as well as new treatment methods for basal cell carcinoma and BCNS. According to Bale, the next step is to determine the biochemical pathways by which the gene mutations lead to cancer. "Understanding the molecular mechanisms underlying skin cancer may enable us to develop rational medical theory," he said, "[for example], a skin cream containing a chemical that replaces the function of the mutant *patched* gene." Bale said his group is working to construct a mouse model for BCNS which will be used to test new medications and to study the role of the *patched* gene in development.